Notice of Allowability	Application No.	Applicant(s)	
	09/673,735	DORKEN ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *11.21.2005*.

2. ☒ The allowed claim(s) is/are *1-5, 7-10, 12-16, 20-23, 30, 33, 37, 40 and 41*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Dr. Richard Peet on 12.05.2005.

3. Claims 11 and 44-45 have been cancelled.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
(571) 272-8789.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) A single-chain multi-functional polypeptide comprising

(a) a first domain comprising a binding-site of an antibody or an immunoglobulin chain thereof specifically recognizing the CD19 antigen; and

(b) a second domain comprising a binding site of an antibody or an immunoglobulin chain thereof recognizing the human CD3 antigen,

wherein said domains are arranged in the order V_LCD19- V_HCD19-V_HCD3-V_LCD3.

2. (Original) The polypeptide of claim 1, wherein said two domains are connected by a polypeptide linker.

3. (Previously Presented) The polypeptide of claim 1, wherein said first and/or second domain correspond to a V_H and V_L region from a natural antibody.

4. (Previously Presented) The polypeptide of claim 1, wherein said antibody is monoclonal antibody, synthetic antibody, or humanized antibody.

5. (Previously Presented) The polypeptide of claim 4, wherein at least one of said domains is a single-chain fragment of the variable region of the antibody.

6. (Canceled)

6 7. (Previously Presented) The polypeptide of claim 2, wherein said polypeptide linker comprises a plurality of glycine, alanine, serine residues or combinations thereof.

7 8. (Previously Presented) The polypeptide of claim 2, wherein said polypeptide linker comprises a plurality of consecutive copies of an amino acid sequence.

8 ~~9~~. (Previously Presented) The polypeptide of claim 2, wherein said polypeptide linker comprises 1 to 5 amino acid residues.

9 ~~10~~. (Previously Presented) The polypeptide of claim 9, wherein said polypeptide linker comprises the amino acid sequence Gly Gly Gly Gly Ser.

11. (Previously Presented) The polypeptide of claim 1, comprising at least one of said first or second domains, wherein said first domain comprises at least one CDR of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 82 to 414 (V_L) and nucleotides 460 to 831 (V_H) and, wherein said second domain comprises at least one CDR of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 847 to 1203 (V_H) and nucleotides 1258 to 1575 (V_L).

10 ~~12~~. (Previously Presented) The polypeptide of claim 1, wherein

(a) said binding site of the first domain has an affinity of at least about 10^{-7} M; and/or

(b) said binding site of the second domain has an affinity of less than about 10^{-7} M.

11 ~~13~~. (Previously Presented) The polypeptide of claim 1, wherein said polypeptide is a bispecific single-chain antibody.

12 ~~14~~. (Previously Presented) The polypeptide of claim 1, comprising at least one further domain.

13 ~~15~~. (Original) The polypeptide of claim 14, wherein said further domain is linked by covalent or non-covalent bonds.

14 ~~16~~. (Previously Presented) The polypeptide of claim 14, wherein said at least one further domain comprises an effector molecule having a conformation suitable for biological activity, capable of sequestering an ion or selective binding to a solid support or to a preselected determinant.

17.-19. (Canceled)

15 ~~20~~. (Previously Presented) A method for the preparation of a single-chain multi-functional polypeptide comprising:

cultivating a cell transfected with a polynucleotide which upon expression encodes the single-chain multi-functional polypeptide of claim 1; and

isolating said polypeptide from the cell.

16 ~~21~~. (Previously Presented) A composition comprising a single-chain multi-functional polypeptide comprising:

(a) a first domain comprising a binding-site of an antibody or an immunoglobulin chain thereof specifically recognizing the CD 19 antigen; and

(b) a second domain comprising a binding site of an antibody or an immunoglobulin chain thereof recognizing the human CD3 antigen,

wherein said domains are arranged in the order V_LCD19- V_HCD19-V_HCD3-V_LCD3.

17 ~~22~~. (Previously Presented) The composition of claim 21 which is a pharmaceutical composition optionally further comprising a pharmaceutically acceptable carrier.

18 ~~23~~. (Original) The composition of claim 21, which is a diagnostic composition optionally further comprising suitable means for detections.

24-29. (Canceled)

19 ~~30~~. (Previously Presented) A method for the treatment of B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells comprising administering to a human afflicted with said malignancies, diseases or depletion, an effective amount of:

a single-chain multi-functional polypeptide comprising:

(a) a first domain comprising a binding-site of an antibody or an immunoglobulin chain thereof specifically recognizing the CD 19 antigen; and

(b) a second domain comprising a binding site of an antibody or an immunoglobulin chain thereof recognizing the human CD3 antigen,
wherein said domains are arranged in the order V_LCD19- V_HCD19-V_HCD3-V_LCD3.

31.-32. (Canceled)

20 ~~33~~. (Previously Presented) The method of claim 30, wherein said B-cell malignancy is non-Hodgkin lymphoma.

34.-36. (Canceled)

21 ~~37~~. (Previously Presented) The method of claim 20, wherein said first and/or second domain correspond to a V_H and V_L region from a natural antibody.

38.-39. (Canceled)

22 ~~40~~. (Previously Presented) The method of claim 20, wherein the single-chain multi-functional polypeptide comprises at least one further domain.

23 ~~41~~. (Previously Presented) The method of claim 30, wherein said first and/or second domain correspond to a V_H and V_L region from a natural antibody.

42.-43. (Canceled)

~~44~~. (Previously Presented) The polypeptide of claim 1, comprising at least one of said first or second domains, wherein said first domain comprises at least two CDRs of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 82 to 414 (V_L) and nucleotides 460 to 831 (V_H) and, wherein said second domain comprises at least two CDRs of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 847 to 1203 (V_H) and nucleotides 1258 to 1575 (V_L).

~~45~~. (Previously Presented) The polypeptide of claim 1, comprising at least one of said first or second domains, wherein said first domain comprises the three CDRs of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 82 to 414 (V_L) and nucleotides 460 to 831 (V_H) and,

wherein said second domain comprises the three CDRs of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 847 to 1203 (V_H) and nucleotides 1258 to 1575 (V_L).